FORM PTO-1390 (Modified) (REV 11-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	
65,213-001	
U.S. APPLICATION NO (IF KNOWN, SEE 37 CFR)	
09/787806	
INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE
PCT/GB99/03196	**24 SEPT 1999**
PRIORITY DATE CLAIMED	
25 SEPT 1998	

TITLE OF INVENTION

NUTRITIONAL AND PHARMACEUTICAL COMPOSITIONS

APPLICANT(S) FOR DO/EO/US

Whittle, Brian Anthony

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ A copy of the International Search Report (PCT/ISA/210).
8. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409)
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☒ Certificate of Mailing by Express Mail
20. ☐ Other items or information:

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/787806	PCT/GB99/03196	65.213-001

21. The following fees are submitted:.

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :	CALCULATIONS	PTO USE ONLY
☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO	$1,000.00	
☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but Internation Search Report prepared by the EPO or JPO	$860.00	
☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	$710.00	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)	$690.00	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)	$100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$860.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).	$130.00	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	11 - 20 =	0	x $18.00	$0.00	
Independent claims	4 - 3 =	1	x $80.00	$80.00	
Multiple Dependent Claims (**check if applicable**).			☐	$0.00	
TOTAL OF ABOVE CALCULATIONS			=	$1,070.00	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) **(check if applicable)**.			☐	$0.00	
SUBTOTAL			=	$1,070.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).			+	$0.00	
TOTAL NATIONAL FEE			=	$1,070.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) **(check if applicable).**			☐	$0.00	
TOTAL FEES ENCLOSED			=	$1,070.00	
				Amount to be: refunded	$
				charged	$

☐ A check in the amount of to cover the above fees is enclosed.

☒ Please charge my Deposit Account No. **04-2223** in the amount of **$1,070.00** to cover the above fees.
A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **04-2223** A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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SIGNATURE

Robert L. Kelly
NAME

31,843
REGISTRATION NUMBER

March 23, 2001
DATE

VERIFIED STATEMENT BY INVENTOR CLAIMING
SMALL ENTITY STATUS (37 C.F.R. 1.9(f) and 1.27(c))

As a below named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees under Section 41(a) and (b) of Title 35, United States Code, to the Patent and Trademark Office with regard to the invention entitled:

NUTRITIONAL AND PHARMACEUTICAL COMPOSITIONS

described in the application for Letters Patent submitted herewith.

I have not assigned, granted, conveyed or licensed and am under no obligation under contract or law to assign, grant, convey or license, any rights in the invention to any person who could not be classified as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

NONE

I acknowledge the duty to file, in this application or patent, notification of any change in status that would result in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent to which this verified statement is directed.

Dated: March 22nd 2001

Brian Anthony Whittle

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65,213-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: WHITTLE, Brian Anthony

Serial No.: PCT/GB99/03196 filed September 24, 1999

U.S. Serial No.: Unassigned - filed herewith

For: NUTRITIONAL AND PHARMACEUTICAL COMPOSITIONS

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination and prior to calculating the filing fee, please amend the claims as follows:

Please amend claims 1, 2, 3, 4, 5, 6, 7 and 8 as follows:

1. A nutritional or pharmaceutical composition comprising one or more water containing components in which the water is releasably bound wherein [one or more anhydrous compounds are] at least one anhydrous compound is mixed in the composition in an amount capable of sequestering any water which may be released from the one or more water containing components to provide a continuous desiccant effect under normal handling conditions.

CERTIFICATE OF MAILING (37 C.F.R. § 1.10)

I hereby certify that this paper is being deposited with the United States Postal Service on March 23, 2001, in an envelope as "Express Mail Post Office to Addressee," Mailing Label No. EF112683171US, and is part of the documents transmitted for entry in the U.S. National Phase under Chapter II, addressed to: Box PCT, Assistant Commissioner for Patents, Washington, DC 20231.

Alesia A. Mungons

Alesia A. Mungons

2. The [A] composition according to claim 1, wherein [the one or more anhydrous compounds are] said at least one anhydrous compound is selected from the group consisting of CaO, [and] anhydrous [or calcined] $MgSO_4$ and calcined $MgSO_4$, and a combination thereof.

3. The [A] composition according to claim 2, wherein both CaO and anhydrous or calcined $MgSO_4$ are present.

4. The [A] composition according to claim [claims] 2 [or 3], wherein the CaO is present in an amount up to 10% by weight of the composition.

5. The [A] composition according to claim [claims] 2 [or 3], wherein anhydrous or calcined $MgSO_4$ is present in an amount up to 10% by weight of the composition.

6. A composition as recited in claim 1 [claimed in any of the preceding claims], which further comprises an acid or a salt thereof and a carbonate and/or bicarbonate or a salt thereof sufficient to cause said composition to effervesce in water.

7. A composition as claimed in claim 6 [any of the preceding claims], wherein said acid or a salt thereof is [comprising] calcium lactate.

8. A composition as claimed in claim 1 [any preceding claims] further comprising a sulphite.

Please add the following new claims:

12. The composition according to claim 3, wherein the CaO is present in an amount up to 10% by weight of the composition.

13. The composition according to claim 3, wherein anhydrous or calcined $MgSO_4$ is present in an amount up to 10% by weight of the composition.

REMARKS

Consideration and allowance are respectfully requested.

Respectfully submitted,

Date: March 23, 2001

By: _____

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DESCRIPTION

NUTRITIONAL AND PHARMACEUTICAL COMPOSITIONS

The present invention relates to nutritional and pharmaceutical compositions.

More particularly it is concerned with improving compositions which due to the presence of an efflorescent component may be unstable and prone to decomposition and/or spoilage.

The release of "bound" water in so called " dry compositions" can activate degenerative reactions for a variety of reasons. In such compositions water may be bound as water of crystallisation. Where the composition contains a salt that has water of crystallisation, variations in temperature can cause release of this bound water. If the composition is contained in a closed environment such as a hermetically sealed sachet, then the water vapour released may subsequently condense and produce a micro environment in which the amount of moisture is sufficient to cause a chemical reaction or microbial spoilage. In the closed environment of a sachet of an effervescent preparation, the presence of moisture can lead to a premature reaction. This is manifested as evolution of gas which in extreme cases "blow" the sachet but more typically leads to a composition with a reduced activity.

Where pharmaceutical and nutritional compositions are known to be

particularly sensitive to the presence of moisture, it is necessary to take precautions to reduce the effects of water vapour. It is thus necessary to carry out production in an environment with a low relative humidity. It is also conventional to include a packaged desiccant in the pack in which the product is enclosed. Typically, desiccants used in such packs contain silica gel enclosed in a cartridge or porous sachet. The capacity of these desiccant sachets is variable, depending for their efficacy on the conditions under which they have been stored previously.

The mobility of water that is "locked up" in a salt as water of crystallisation is a problem affecting the stability of nutritional and pharmaceutical compositions.

It is an aim of the present invention to provide a nutritional or pharmaceutical composition which is less prone to decomposition and/or spoilage.

According to a first aspect of the present invention there is provided a nutritional or pharmaceutical composition comprising one or more water containing components in which the water is releasably bound wherein one or more anhydrous compounds are mixed in the composition in an amount capable of sequestering any water which may be released from the one or more water containing components to provide a continuous desiccant effect under normal handling conditions.

The one or more anhydrous compounds and/or their hydrated forms should themselves be nutritionally or pharmaceutically acceptable.

Preferably the one or more anhydrous compounds are selected from CaO and anhydrous or calcined $MgSO_4$.

Since calcium salts have a constipating action and magnesium salts have the

opposite effect it is preferred to incorporate both calcium and magnesium salts to counter their individual effects.

More preferably still the calcium and magnesium present in the composition are present together, more preferably still in the form of CaO and anhydrous or calcined $MgSO_4$.

Preferably the calcium and magnesium in the product are present in amounts sufficient to provide a recommended daily allowance of calcium and magnesium.

Preferably the CaO is present in an amount of up to 10% of the composition (by weight) and more preferably still from 4-8%.

Preferably the magnesium is present as anhydrous or calcined $MgSO_4$.

Preferably the anhydrous or calcined $MgSO_4$ is present in an amount of up to 10% of the composition (by weight) and more preferably still from 1-5%.

The problem of stability is particularly acute where the composition is intended to effervesce.. Such compositions contain an acid, usually in the form of a salt and a carbonate or bicarbonate. The effervescence is caused by a reaction between the acid and carbonate or bicarbonate when the composition is dissolved in water. These compositions, which are often packaged in sachets, are particularly prone to decomposition as the acid salt used, frequently a fruit acid salt, is often calcium lactate, a pentahydrate. The water of crystallisation effloresces causing release of CO_2 and "blowing" of the sachets. By intimately mixing the composition with one or more nutritionally or pharmaceutically

acceptable anhydrous compounds in amounts capable of sequestering any water which may be released from the one or more water containing components of the composition a continuous desiccant effect is provided and the problem is overcome.

Preferably the compositions will include a component, for example, a sulphide, which releases SO_2 in the presence of free water. This has an antimicrobial effect on the composition.

In one embodiment the one or more anhydrous compounds are provided in the form of a premix.

According to a further aspect of the present invention there is provided a composition premix comprising an acid or salt thereof in admixture with an anhydrous compound which has a greater avidity for water than the acid or salt thereof.

According to yet a further aspect of the present invention there is provided the use of CaO and/or anhydrous or calcined $MgSO_4$ in the manufacture of a nutritional or pharmaceutical composition for the purpose of effectively removing/mopping up adventitious water.

The use of such compounds in the manufacture of nutritional and pharmaceutical products means manufacturing can be simplified and costs reduced.

According to yet a further aspect of the present invention there is

provided a method of manufacturing a nutritional or pharmaceutical composition comprising one or more components which contain water which is releasably

bound wherein the manufacturing steps are conducted in the absence of special low humidity conditions and one or more anhydrous compounds are intimately mixed in the product in an amount capable of sequestering any water which may be released from the water containing components to provide a continuous desiccant effect.

The various aspect of the invention will now be described, by way of example only, with reference to the following example compositions and supporting data.

The method of preserving compositions so that they have optimum stability is illustrated by the following examples.

Carbonates and bicarbonates of group I and group II alkali metal elements and ammonia (referred to here as base components) react with acids to give carbon dioxide, and they are the basis of effervescent products when added to water. Pharmaceutically and nutritionally acceptable carbonates that can be used in effervescent compositions are carbonates and acid carbonates of ammonia, lithium, sodium, potassium, calcium and magnesium. Suitable fruit acids are illustrated by (but not limited to) citric, malic, fumaric, tartaric, ascorbic, and lactic acid. The acid component may be a partially neutralised salt of an acid having more than one acidic group. Some of the fruit acids contain water of crystallisation.

Thus, for example citric acid monohydrate contains water of crystallisation which can be driven off by heating. In tests 5.1% by weight of water is driven off on heating to 105°C. The amount of water is sufficient to cause instability in

sachet preparations where the dose amount is confined in a sealed space and subject to variations of temperature.

Table 1 shows the rate of loss of water from some efflorescent salts, and other compounds when weighed quantities were dried in a temperature controlled oven at 105°C for two hours, removed from the oven and allowed to cool in a desiccator before re-weighing.

TABLE 1

COMPOUND	**Percentage weight loss on drying at 105°C** Time in Hours			
	0	1	2	3
Calcium Ascorbate	0	4.9	6.5	7.7
Calcium Lactate (Pentahydrate)	0	24.1	24.2	23.7
Calcium Lactate/Lactic acid adduct	0	40.6	48.8	49.4
Calcium Lactate (Anhydrous)	0	1.5	2.8	3.6
Calcium Oxide	0	-1.3	-4.2	-6.3*
Calcium Hydroxide	0	1.8	2.9	3.2

Calcium Sulphate	0	19.1	21.3	21.5
Magnesium Sulphate (heptahydrate)	0	42.3	44.1	43.4
Magnesium Sulphate (anhydrous)	0	-0.9	1.1	-2.29*

* A negative value indicates an increase in weight

The results show that anhydrous magnesium sulphate takes up moisture even in the drying conditions obtaining in an oven at 105°C. Under the same conditions moisture locked up as water of crystallisation in magnesium sulphate heptahydrate is removed. Similarly, calcium oxide absorbs moisture even when dried in an oven at 105°C.

Calcium lactate, and lactic acid adduct is a proprietary product made by adding calcium carbonate to an 88% solution of Lactic Acid. This gives a crystalline material that corresponds to the pentahydrate, and not to the anhydrous form.

Table 2 illustrates the loss of water from magnesium sulphate heptahydrate, and the temperature at which loss of water occurs.

TABLE 2

Loss of Water from Magnesium Heptahydrate on heating

Temperature °C	No. of molecules of water lost

Ambient	1
70-80°C	4
00°C	5
20°C	6
250°C (Calcined)	7

It shows the progressive effect of heating on the loss of water of crystallisation, and the efficacy of magnesium sulphate is greatest when all of the water has been removed. At a lesser degree of dehydration (when the average weight of water of crystallisation corresponds to more than one molecule of water per molecule of magnesium sulphate) the drying effect of magnesium sulphate is reduced. It is optimal when material is dried or calcined at a temperature greater than 120°C. This anhydrous $MgSO_4$ contains less than, on average, one molecule of water whereas calcined $MgSO_4$ has had substantially all of the water of crystallisation driven off.

Incorporation of dried magnesium sulphate as a magnesium source, in combination with a soluble calcium salt, provides a nutritionally acceptable material that is not hygroscopic, under normal manufacturing conditions.

EXAMPLE METHODS

A solution of calcium lactate is sprayed into the top of a drying tower in which the temperature of the air is 220-250°C. Water in the injected droplets reaches boiling point instantaneously and the latent heat of vaporisation reduces the temperature of the resulting solids. Typically, the temperature of the spray-dried

solids is 40-50°C at the base of the column, and the dwell-time for particles in the spray-dryer is 3-10 seconds. The resulting spray-dried calcium lactate contains 4% of water, i.e., it consists principally of the anhydrous salt. The powder is removed into a drum capable of being sealed and 5.5% of freshly calcined magnesium sulphate is added to the powder and thoroughly mixed. The amount of magnesium sulphate added is in excess of the amount required to sequester water and provides a continuing desiccant effect under normal handling conditions. The amount can be calculated in accordance with the theoretical desiccant activity set out below.

Calcium lactate may also be prepared from ethyl lactate. The calculated amount of ethyl lactate is stirred into a suspension of calcium oxide in ethanol with vigorous stirring. The white solid is removed from the supernatant and dried in a fluid bed dryer. The resulting powder contains anhydrous calcium lactate and calcium hydroxide. Ethyl lactate is volatile (bp 154 °C) and is removed during drying or solvent recovery.

THEORETICAL DESICCANT ACTIVITY

1. $MgSO_4+7H_20$

119 g of Mag Sulph Exsicc. will take up 7 moles (126 g) of water of crystallisation.

1 g of Mag Sulph Exsicc. will take up 126/119g = 1.059 g water, and provides 23/119 x 1000 = 193.3 mg of Mg.

2. $Ca0 + H_20 = Ca(OH)_2$

56 g of Ca0 reacts with 18 g of H_20

1 g of CaO reacts with 18/56 = 0.3214 g water, and provides 40/56 x 1000 = 714.3 mg Ca.

3. 1 g of calcium lactate pentahydrate (CAPH) contains 25% water = 250 mg

4. 1 g of anhydrous calcium lactate (CL) contains (say) 4% water = 40 mg of water.

5. To mop up the water in 1 g of CL requires

a) For anhydrous CL - 40 x 1.059 x 1000 = 42.36 mg $MgSO_4$

b) For CLPH - 250/1.059 x 1000 = 264.8 mg $MgSO_4$

c) For anhydrous CL - 40 x 0.7143 = 28.57 mg CaO

d) For CLPH - 250 x 0.7143 = 178.6 mg CaO

EXAMPLE 1

A compound electrolyte powder containing calcium lactate (as the pentahydrate) tends to "cake" on storage at ambient temperature in the absence of a desiccant bag. One method of minimising caking is to store the composition in well-sealed containers containing a desiccant bag of a drying agent such as silica gel. In the preparation of effervescent tablets it is necessary to carry out manufacture in an environment with a low relative humidity. A free flowing powder which can be used in manufacture using normal handling conditions can be made by extracting most of the water of crystallisation and locking up the remainder by admixture with an anhydrous compound which has greater avidity for water than calcium lactate.

Calcium lactate is a preferred source of calcium in nutritional compositions

and compositions which are "anhydrous" or have a low concentration of water they can be prepared by the following methods:

1. Spray-drying a saturated solution/suspension of calcium lactate pentahydrate. Drying calcium lactate pentahydrate at a temperature of 90-110°C. This temperature does not cause decomposition or chemical rearrangement, or

2. By reacting calcium oxide with ethyl lactate in a non aqueous solvent such as ethanol or n-propanol.

The "anhydrous" calcium lactate produced by one of the processes described above is immediately mixed intimately with up to 10% (and preferably 1 - 5%) of dried magnesium sulphate and/or up to 10% (and preferably 4-8%) of calcium oxide. The amounts of magnesium sulphate and/or calcium oxide are in excess of the amount required to sequester the calculated amount of residual moisture and this will provide a continuing desiccant effect under normal handling conditions.

The resulting powder is referred to as "compound calcium lactate powder" (CCLP) in the following examples. CCLP may be used as a constituent in the formulation of other solid dose form compositions. In the following examples a powder containing magnesium sulphate (1.8%) and calcium oxide (5.8%) is used to illustrate the method. The "anhydrous" calcium lactate accounts for the remainder of the composition. The recommended daily allowance of calcium and magnesium vary from country to country and the quantitative composition of the compound powder can be adjusted to meet specific manufacturing requirements by

the skilled man using the teaching of this example.

Example 2 is a formulation providing powder for preparation of an effervescent drink.

EXAMPLE 2

A compound powder is prepared by mixing the following. Quantities are by weight and 5.9 g of the powder is sufficient to provide 100% of the RDA of calcium, 20% of the RDA of magnesium, and 100% of the RDA of ascorbic acid. This composition is a powder to be used, when added to water, as an effervescent drink.

Spray-dried powder as described in Example 1	1.1g
Anhydrous calcium ascorbate	0.1g
Anhydrous citric acid	3.0g
Sodium bicarbonate	1.0g
Magnesium carbonate	0.2g
Precipitated calcium carbonate	1.5g

Portions of 6.9g are dispensed into laminated foil sachets and sealed in the conventional manner. The sachets are stable enough to support a shelf life claim of at least 1-year at ambient temperature. When required for use, the contents of the sachet are added to approximately 150-200 ml of water and stirred to produce a refreshing effervescent calcium-enriched drink.

EXAMPLE 3

A compound mineral and multivitamin powder is prepared by mixing the following. Quantities are by weight and 7.13g of the powder is sufficient to provide 100% of the RDA of calcium 20% of the RDA of magnesium, and 100% of the RDA of Vitamins A, B, C, D and E together with trace elements for which RDAs have not been determined. It is conventional to use a commercially available blend of vitamins.

Vitamin blended powder	1.0g
Spray-dried powder as described in Example 1	1.5g
Anhydrous calcium ascorbate	0.1g
Anhydrous citric acid	3.0g
Sodium bicarbonate	1.0g
Magnesium carbonate	0.18g
Calcium carbonate (precipitated)	1.3g
Zinc Sulphate	0.05g
Ferrous Sulphate	0.01g
Copper Sulphate	0.002g
Selenium Yeast Complex	0.001g
Manganese Sulphate	0.001g
	7.644g

Portions of 7.644g are dispensed into laminated foil sachets and heat-sealed in the conventional manner. The sachets are stable enough to support a shelf-life claim of at least 1-year at ambient temperature. When required for use, the

contents of the sachet are added to approximately 150ml of water and stored to produce a refreshing effervescent drink.

EXAMPLE 4

A compound powder is prepared by mixing the following components. Quantities are given by weight. Twelve grams of the powder is sufficient to provide 100% of the RDA of calcium, 20% of the RDA of magnesium, and 100% of the RDA of ascorbic acid.

Spray-dried powder as described in Example 1	10.0g
Anhydrous Malic Acid	8.0g
Sodium benzoate	0.175g
Asesulfame	0.15g
Aspartame	0.07g

To prepare a carbonated drink, 19.3kg of this powder is dissolved in 1000 litres of potable water, filtered, sterilised by UV radiation and carbonated with up to 4 volumes of carbon dioxide. The mineralised water so produced provides 100% of the RDA of calcium and 20% of the RDA of magnesium.

EXAMPLE 5

A compound powder is prepared by mixing the following components. The quantities are given by weight.

Compound Calcium Lactate Powder as described in Example 1	6.4g
Anhydrous Malic Acid	5.0g
Light Magnesium carbonate BP	0.75g

When 12.15 kg of this powder is dissolved in 1000 litres of water,

mineralised water is produced to which can be added fruit flavours, fruit juices, colours sweeteners and optionally, carbon dioxide to provide a mineral enriched drink. 600 ml of this drink will provide 100% of the RDA of calcium and 40% of the RDA of magnesium.

EXAMPLE 6

A concentrate for preparation of a mineralised hot drink is prepared by mixing the following.

Powder described in Example 1	28.7g
Concentrated mixed fruit juice (8x)	150g
Calcium Sulphite (Anhydrous)	0.1g
Flavouring	0.2g

The mixture is heated and kept at a temperature of 110°C, for 5 minutes, allowed to cool to 60°C, 20 ml quantities filled into sachets and sealed. For use, the contents of the sachet are dissolved in 150 ml of water to provide a refreshing and comforting drink containing 75% of the RDA of calcium, 100% of the RDA of Vitamin C and 20% of the RDA of magnesium.

The premix, CCLP, can be used to mineralise confectionary, Traditionally, confectionery products contain sucrose or corn syrup as a sweetening agent. Both of these substances leave a residue of sugar in the saliva which will be subject to bacterial degradation and acidification. The products of degradation may result in tooth decay (dental caries) which is particularly serious in children. It has been

found that confectionery products of a type popular with young children can be fortified with minerals without loss of palatability. The powder described in Example 1 can be used to provide a re-mineralising concentration of calcium and magnesium, and is a contribution to the prevention of dental caries in young children. The methods of manufacture of confectionery will be familiar to the man skilled in the art, particularly those relating to qualative and quantative aspects of flavour and sweetness. These can be modified within the teaching of the disclosure to produce mineral supplements suitable for particular therapeutic needs.

CLAIMS

1. A nutritional or pharmaceutical composition comprising one or more water containing components in which the water is releasably bound wherein one or more anhydrous compounds are mixed in the composition

in an amount capable of sequestering any water which may be released from the one or more water containing components to provide a continuous desiccant effect under normal handling conditions.

2. A composition according to claim 1, wherein the one or more anhydrous compounds are selected from CaO and anhydrous or calcined $MgSO_4$.

3. A composition according to claim 2, wherein both CaO and anhydrous or calcined $MgSO_4$ are present.

4. A composition according to claims 2 or 3, wherein the CaO is present in an amount up to 10% by weight of the composition.

5. A composition according to claims 2 or 3, wherein anhydrous or calcined $MgSO_4$ is present in an amount up to 10% by weight of the composition.

6. A composition as claimed in any of the preceding claims, which further comprises an acid or a salt thereof and a carbonate and/or bicarbonate or a salt thereof.

7. A composition as claimed in any of the preceding claims, comprising calcium lactate.

8. A composition as claimed in any preceding claims further comprising

a sulphite.

9. A composition premix comprising an acid or salt thereof in admixture with an anhydrous compound which has a greater avidity for water than the acid or salt thereof.

10. The use of CaO and/or anhydrous or calcined $MgSO_4$ in the manufacture of a nutritional or pharmaceutical composition for the purpose of effectively removing/mopping up adventitious water.

11. A method of manufacturing a nutritional or pharmaceutical composition comprising one or more components which contain water which is releasably bound wherein the manufacturing steps are conducted in the absence of special low humidity conditions and one or more anhydrous compounds are intimately mixed in the product in an amount capable of sequestering any water which may be released from the water containing components to provide a continuous desiccant effect.

INTERNATIONAL SEARCH REPORT

Ir. ational Application No
PCT/GB 99/03196

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A23L2/39 A23L2/44 A61K33/06 A61K33/32 A61K47/02
A23L2/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A23L A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 96 22704 A (TAKAICHI) 1 August 1996 (1996-08-01) page 2, line 18 - line 24 page 3, line 9 - line 16 page 6, line 11 - line 15 example A claims 1,2,5	1,2,4, 9-11 7
X	US 2 297 599 A (WILLEN) 29 September 1942 (1942-09-29) examples 1-3	1,2,5,6, 11
X A	DE 38 26 903 A (WILLHELM) 15 February 1990 (1990-02-15) column 3, line 15 - line 23 claims 1,4,5,8,10,11	1,2,4,5, 10,11 3,7
	-/—	-

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 January 2000	28/01/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Lepretre, F

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/03196

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 040 654 A (VITAPHARM PHARMACEUTICAL PTY LTD.) 2 December 1981 (1981-12-02) claims 9,10; examples	1,2,5,9, 11
X	WO 94 20077 A (BÉRES RÉSZVENYTÀRASASÀG) 15 September 1994 (1994-09-15)	9,11
A	page 3, line 23 - line 31 page 7, line 16 - line 24 claims 1,6,7	1,6,7
A	PATENT ABSTRACTS OF JAPAN vol. 008, no. 003 (C-203) & JP 58 170464 A (NISSAN KAGAKU) abstract	2-5,10
A	EP 0 400 460 A (SAKASI CHEMICALS) 5 December 1990 (1990-12-05) claim 1	2-5,10

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

In ational Application No
PCT/GB 99/03196

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9622704 A	01-08-1996	JP 8196247 A	06-08-1996
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		JP 3109916 A	09-05-1991
		JP 7053222 B	07-06-1995

Table 1

	Specimen oil 1	Specimen oil 2	Specimen oil 3	Comparative oil 1	Comparative oil 2
Viscosity (mm^2/s) at 100℃	2.4	5.0	10.5	1.0	12.3
Compatibility with refrigerant High temperatur 2-phase separation temperature ・Oil percentage : 10 wt %	110℃ or more	95℃	100℃	110℃ or more	Separated at room temperature
・Oil percentage : 3 wt %	110 ℃ or more	100℃	−105℃	110℃ or more	Separated at room temperature
Low temperature 2-phase separation temperature ・Oil percentage : 10 wt %	−40℃ or less	−20℃	−40℃ or less	−40℃ or less	Separated at room temperature
Hygroscopic property (Moisture %) 7 days	0.04	0.06	0.09	0.02	−
14 days	0.08	0.10	0.17	0.05	−
21 days	0.13	0.16	0.27	0.10	−
28 days	0.17	0.22	0.32	0.13	−
Thermal stability 140℃ × 24 hr Evaporation loss	Low	Low	Low	High	Low

Docket No. 65,213 -001
PATENT

COMBINED DECLARATION AND POWER OF ATTORNEY
(Entry into the National Phase of an International Application in the United States of America)

I, the undersigned inventor, hereby declares that:

My residence, post office address, and citizenship are as stated next to my name below;

I believe that I am the first and original inventor of the subject matter claimed in the application for patent entitled NUTRITIONAL AND PHARMACEUTICAL COMPOSITIONS which is described and claimed in the U.S. Patent Application, enclosed herewith;

I have reviewed and understand the contents of the above-identified application for patent (hereinafter "the application"), including the claims;

I acknowledge the duty under Title 37, Code of Federal Regulations, Section 1.56(a), to disclose information known to be material to the patentability of this application. I also acknowledge that information is material to patentability when it is not cumulative to information already provided to the United States Patent and Trademark Office and when it either

compels, by itself or in combination with other information, a conclusion that a claim is unpatentable under the preponderance of evidence standard, before any consideration is given to evidence which may be submitted to establish a contrary conclusion of patentability, or

refutes or is inconsistent with a position taken in either (i) asserting an argument of patentability, or (ii) opposing an argument of unpatentability relied on by the United States Patent and Trademark Office;

I hereby claim the priority benefit under Title 35, Section 365(c), of the following PCT International Patent Application designating the United States:

Application No.	Filing Date	Based on
PCT/GB99/03196	24 Sept 1999	UK Patent Application 9820815.0 (filed on 25 Sept 1998)

Where the subject matter of the claims of this application is not disclosed in the priority PCT International Application, I acknowledge the duty to disclose information known to be material to the patentability of this application that became available between the filing dates of this application and of the priority PCT International Application;

65,213-001

I hereby appoint as my attorneys with full power of substitution to prosecute this application and conduct all business in the United States Patent and Trademark Office associated with this application the firm of DYKEMA GOSSETT PLLC, including Charles R. Rutherford, Reg. No. 18,933, Robert L. Kelly, Reg. No. 31,843, Ernest E. Helms, Reg. No. 29,721, Kevin M. Hinman, Reg. No. 35,193, John W. Rees, Reg. No. 38,278, William F. Kolakowski III, Reg. No. 41,908, Adam B. Strauss, Reg. No. 43,167, and Maryann Pierce Pertunnen, Reg. No. 46,987, located at 39577 North Woodward Avenue, Suite 300, Bloomfield Hills, Michigan 48304-2820.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

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Signature of Inventor

Date 22nd March 2001

Citizenship: Great Britain
Residence: Same

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